ClinicalEvidence

Bacterial conjunctivitis

Search date July 2009

John Epling

ABSTRACT

INTRODUCTION: Most cases of conjunctivitis in adults are probably due to viral infection, but children are more likely to develop bacterial conjunctivitis than they are viral forms. The main bacterial pathogens are Haemophilus influenzae and Streptococcus pneumoniae in adults and children, and Moraxella catarrhalis in children. Contact lens wearers may be more likely to develop gram-negative infections. Bacterial keratitis occurs in up to 30 per 100,000 contact lens wearers. METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical questions: What are the effects of empirical treatment in adults and children with suspected bacterial conjunctivitis? What are the effects of treatment in adults and children with bacteriologically confirmed bacterial conjunctivitis? What are the effects of treatment in adults and children with clinically confirmed gonococcal conjunctivitis? We searched: Medline, Embase, The Cochrane Library, and other important databases up to July 2009 (Clinical Evidence reviews are updated periodically; please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA). RESULTS: We found 40 systematic reviews, RCTs, or observational studies that met our inclusion criteria. We performed a GRADE evaluation of the quality of evidence for interventions. CONCLUSIONS: In this systematic review we present information relating to the effectiveness and safety of the following interventions: ocular decongestants; oral antibiotics; parenteral antibiotics; saline; topical antibiotics; and warm compresses.

QUESTIONS

What are the effects of empirical treatment in adults and children with suspected bacterial conjunctivitis?. . . . 3

What are the effects of treatment in adults and children with bacteriologically confirmed bacterial conjunctivitis?. 6

What are the effects of treatment in adults and children with clinically confirmed gonococcal conjunctivitis?. . . 8

INTERVENTIONS

TREATMENTS FOR SUSPECTED BACTERIAL CONJUNCTIVITIS

Likely to be beneficial

Empirical treatment with topical antibiotics in people with suspected bacterial conjunctivitis (given to patient with advice to use after 1–2 days if symptoms do not resolve) 3

Unknown effectiveness

Empirical treatment with ocular decongestants in people with suspected bacterial conjunctivitis 6

Empirical treatment with oral antibiotics in people with suspected bacterial conjunctivitis 5

Empirical treatment with saline in people with suspected bacterial conjunctivitis 6

Empirical treatment with warm compresses in people with suspected bacterial conjunctivitis 6

TREATMENTS FOR CONFIRMED BACTERIAL CONJUNCTIVITIS

Beneficial

Antibiotics (topical) in people with culture-positive non-gonococcal bacterial conjunctivitis 6

Unknown effectiveness

Ocular decongestants in people with confirmed bacterial conjunctivitis 8

Saline in people with confirmed bacterial conjunctivitis 8

Warm compresses in people with confirmed bacterial conjunctivitis 8

TREATMENTS FOR GONOCOCCAL CONJUNCTIVITIS

Likely to be beneficial

Antibiotics (parenteral alone or combined with topical) in people with suspected or confirmed gonococcal conjunctivitis)* 8

Unknown effectiveness

Antibiotics (oral) in people with suspected or confirmed gonococcal conjunctivitis 9

Ocular decongestants in people with suspected or confirmed gonococcal conjunctivitis 9

Saline in people with suspected or confirmed gonococcal conjunctivitis 10

Warm compresses in people with suspected or confirmed gonococcal conjunctivitis 10

To be covered in future updates

Antibiotics in people with culture-positive gonococcal bacterial conjunctivitis

Antibiotics in people with acanthamoeba keratitis

Combination treatments in people with acanthamoeba keratitis

Propamidine isethionate

Footnote

*Categorisation based on consensus

Key points

- Conjunctivitis causes irritation, itching, foreign body sensation, and watering or discharge of the eye.

  Most cases in adults are probably due to viral infection, but children are more likely to develop bacterial conjunctivitis than viral forms. The main bacterial pathogens are *Staphylococcus* species in adults, and *Haemophilus influenzae*, *Streptococcus pneumoniae*, and *Moraxella catarrhalis* in children.

  A bacterial cause is more likely if there is glueing of the eyelids and no itch.

  Contact lens wearers may be more likely to develop gram-negative infections. Bacterial keratitis occurs in up to 30/100,000 contact lens wearers.

  Gonococcal ophthalmia neonatorum can occur in up to 10% of infants exposed to gonorrhoeal exudate during delivery despite prophylaxis, and can be associated with bacteraemia and meningitis.

  Otitis media can occur in 25% of children with *H influenzae* conjunctivitis, and meningitis can develop in 18% of people with meningococcal conjunctivitis.

- Conjunctivitis resolves spontaneously within 2 to 5 days in more than half of people without treatment, but infectious complications can occur rarely.

- Topical antibiotics may speed up clinical and microbiological cure of bacterial conjunctivitis, but the benefit is small.

  In people with suspected, but not confirmed, bacterial conjunctivitis, empirical treatment with topical antibiotics may be beneficial. However, this benefit is marginal, so it is advisable to suggest that patients take antibiotics only if symptoms do not resolve after 1 to 2 days.

  Clinical and microbiological cure rates are increased in the first week in people with culture-positive bacterial conjunctivitis, but there is no good evidence of a longer-term benefit from topical antibiotics.

  Adverse effects of topical antibiotics are mild, but their effect on bacterial resistance is unknown.

- Parenteral antibiotics may cure gonococcal ophthalmia neonatorum, although we don't know whether they are beneficial in children in developed countries, as we only found studies from Africa. Neonates will usually require investigation for concomitant infections and complications.

  We don't know whether ocular decongestants, saline, or warm compresses are beneficial in people with suspected or confirmed bacterial or gonococcal conjunctivitis.

DEFINITION

Conjunctivitis is any inflammation of the conjunctiva, generally characterised by irritation, itching, foreign body sensation, and watering or discharge. Treatment is often based on clinical suspicion that the conjunctivitis is bacterial, without waiting for the results of microbiological tests. In this review, therefore, we have distinguished the effects of empirical treatment from effects of treatment in people with culture-positive bacterial conjunctivitis. Bacterial conjunctivitis in contact lens wearers is of particular concern because of the risk of bacterial keratitis — an infection of the cornea accompanying acute or subacute corneal trauma, which is more difficult to treat than conjunctivitis and can threaten vision. [1] [2] Conjunctivitis caused by *Neisseria gonorrhoeae* — referred to as ophthalmia neonatorum — is primarily a disease of neonates, caused by exposure of the neonatal conjunctivae to the cervico-vaginal exudate of infected women during delivery. [3] **Diagnosis** The traditional criteria differentiating bacterial from other types of conjunctivitis have been: a yellow–white mucopurulent discharge; a papillary reaction (small bumps with fibrovascular cores on the palpebral conjunctiva, appearing grossly as a fine velvety surface); and bilateral infection. One systematic review was unable to find any quality research basis for these criteria, [4] but a follow-up study performed by the authors of the review found that glued eyes and the absence of itching were predictive of a bacterial cause. [5] A history of recent conjunctivitis argued against a bacterial cause. If eye pain is moderate or severe and visual acuity is reduced, more serious causes need to be considered. Gonococcal ophthalmia neonatorum is diagnosed by a persistent and increasingly purulent conjunctivitis in exposed infants, beginning from 3 to 21 days after delivery. [3]

INCIDENCE/ PREVALENCE

We found no good evidence on the incidence or prevalence of bacterial conjunctivitis. Bacterial keratitis is estimated to occur in 10 to 30/100,000 contact lens wearers. [6] Gonococcal ophthalmia neonatorum occurs at rates of 0% to 10% in infants who received antibiotic prophylaxis after delivery to mothers with gonorrhoea infection, and in 2% to 48% of exposed infants without prophylaxis. [3]

AETIOLOGY/ RISK FACTORS

Conjunctivitis may be infectious (causes include bacteria and viruses) or allergic. In adults, bacterial conjunctivitis is less common than viral conjunctivitis, although estimates vary widely (viral conjunctivitis has been reported to account for 8% to 75% of acute conjunctivitis). [7] [8] [9] *Staphylococcus* species are the most common pathogens for bacterial conjunctivitis in adults, followed by *Streptococcus pneumoniae* and *Haemophilus influenzae*. [10] [11] In children, bacterial conjunctivitis is more common than the viral form, and is mainly caused by *H influenzae*, *S pneumoniae*, and *Moraxella catarrhalis*. [12] [13] One prospective study (428 children from southern Israel with a clinical diagnosis of conjunctivitis) found that in 55% of the children, conjunctivitis was caused

by *S pneumoniae*, *H influenzae*, or *M catarrhalis*. [14] Narrative reviews suggest that the causative agents of bacterial conjunctivitis and keratitis in contact lens wearers are more frequently gram-negative bacteria (such as *Pseudomonas aeruginosa*), but may include all of the above agents. *Acanthamoeba spp.* infections can be particularly difficult to diagnose and treat, and are most common in contact lens wearers. [1] [2]

PROGNOSIS

Most bacterial conjunctivitis is self-limiting. One systematic review (search date 2004) found clinical cure or significant improvement with placebo within 2 to 5 days in 65% of people. [15] Some organisms cause corneal or systemic complications, or both. Otitis media may develop in 25% of children with *H influenzae* conjunctivitis, [16] and systemic meningitis may complicate primary meningococcal conjunctivitis in 18% of people. [17] Untreated gonococcal ophthalmia neonatorum can cause corneal ulceration, perforation of the globe, and panophthalmitis. Investigations to detect concomitant infections, as well as gonococcal bacteraemia and meningitis, and admission to hospital for parenteral treatment of the eye infection, are frequently required.

AIMS OF INTERVENTION

To achieve rapid cure and to prevent complications of infection, with minimum adverse effects of treatment.

OUTCOMES

Time to cure or improvement. **Clinical signs/symptoms:** hyperaemia, discharge, papillae, follicles, chemosis, itching, pain, and photophobia. Most studies used a numbered scale to grade signs and symptoms. Some studies also included evaluation by investigators and participants regarding success of treatment. **Culture results:** These are proxy outcomes, usually expressed as the number of colonies, sometimes with reference to a threshold level. Results were often classified into categories such as eradication, reduction, persistence, and proliferation.

METHODS

Clinical Evidence search and appraisal July 2009. The following databases were used to identify studies for this systematic review: Medline 1966 to July 2009, Embase 1980 to July 2009, and The Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Clinical Trials Issue 3, 2009. Additional searches were carried out using these websites: NHS Centre for Reviews and Dissemination (CRD) — for Database of Abstracts of Reviews of Effects (DARE) and Health Technology Assessment (HTA), Turning Research into Practice (TRIP), and NICE. Abstracts of the studies retrieved from the initial search were assessed by an information specialist. Selected studies were then sent to the author for additional assessment, using pre-determined criteria to identify relevant studies. Study design criteria for inclusion in this review were: published systematic reviews and RCTs in any language, containing more than 20 individuals of whom more than 80% were followed up. There was no minimum length of follow-up required to include studies, and we included open-label studies. In addition, we use a regular surveillance protocol to capture harms alerts from organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA), which are added to the reviews as required. To aid readability of the numerical data in our reviews, we round many percentages to the nearest whole number. Readers should be aware of this when relating percentages to summary statistics such as relative risks (RRs) and odds ratios (ORs). The categorisation of the quality of the evidence (high, moderate, low, or very low) reflects the quality of evidence available for our chosen outcomes in our defined populations of interest. These categorisations are not necessarily a reflection of the overall methodological quality of any individual study, because the *Clinical Evidence* population and outcome of choice may represent only a small subset of the total outcomes reported, and population included, in any individual trial. For further details of how we perform the GRADE evaluation and the scoring system we use, please see our website (www.clinicalevidence.com). We have performed a GRADE evaluation of the quality of evidence for interventions included in this review (see table, p 21).

QUESTION **What are the effects of empirical treatment in adults and children with suspected bacterial conjunctivitis?**

OPTION **EMPIRICAL TREATMENT WITH TOPICAL ANTIBIOTICS IN PEOPLE WITH SUSPECTED BACTERIAL CONJUNCTIVITIS**

Cure rates

Compared with placebo or no immediate treatment Topical antibiotics may be more effective at improving microbiological cure rates at 2 to 7 days, but we don't know about clinical cure rates as results varied between RCTs depending on the topical antibiotic used and the analysis undertaken (low-quality evidence).

Compared with each other We don't know whether any one topical antibiotic is consistently more effective than the others at improving clinical or microbiological cure (low-quality evidence).

Compared with oral antibiotics We don't know whether polymyxin B sulphate–bacitracin ointment is more effective than oral cefixime at improving clinical cure or bacteriological failure rates in children aged 2 months to 6 years with suspected bacterial conjunctivitis (very low-quality evidence).

Different regimens compared with each other We don't know whether topical gatifloxacin applied twice daily is more effective than topical gatifloxacin applied four times daily at increasing clinical cure at 5 days (low-quality evidence).

Note
Topical antibiotics are associated with burning, stinging, and bad taste.

For GRADE evaluation of interventions for bacterial conjunctivitis, see table, p 21 .

Benefits:

Topical antibiotics versus placebo or no immediate treatment:
We found one systematic review [15] and one subsequent RCT. [18] The systematic review (search date 2005; 3 RCTs; 791 people with suspected bacterial conjunctivitis) compared topical antibiotics (norfloxacin, fusidic acid, and chloramphenicol) versus placebo. [15] The review performed a meta-analysis including RCTs of both suspected and confirmed culture-positive bacterial conjunctivitis, but did not perform separate meta-analyses for these populations; we therefore report results of the individual RCTs here. Two RCTs identified by the review found no significant difference in clinical cure between topical antibiotics and placebo at 3 or 7 days. [19] [20] One RCT found that topical antibiotics significantly increased clinical cure at 5 days compared with placebo. Cure rates after 5 days were generally high in both treatment groups (see table 1, p 13). [11] The subsequent RCT (307 adults and children with acute bacterial conjunctivitis diagnosed clinically by general practitioners) compared three interventions: chloramphenicol drops prescribed immediately, chloramphenicol drops prescribed in a "delayed" fashion (to be used in 2–3 days after diagnosis at the patient's discretion for worsening or persistent symptoms), and no antibiotics. The RCT used a symptom score ranging from 0 for normal to 6 for severe (which included red eye, eye discomfort, daytime eye discharge, sticky eye on waking, eyelid swelling, altered vision, and how unwell the person felt). The RCT found that both immediate and delayed antibiotics significantly reduced the duration of moderate symptoms compared with no antibiotics (see table 1, p 13). However, it found no significant difference between immediate or delayed antibiotics and no antibiotics in symptom scores after 1 to 3 days (symptom score: 1.9 with immediate antibiotics *v* 2.1 with no antibiotics; P = 0.2; symptom score: 2.0 with delayed antibiotics *v* 2.1 with no antibiotics; P = 0.4). [18]

Topical antibiotics versus each other:
We found no systematic review but found 23 RCTs (4 published in the same article) [21] conducted in adults and children (see table 1, p 13). [22] [23] [24] [21] [25] [26] [27] [28] [29] [30] [31] [32] [33] [34] [35] [36] [37] [38] [39] [40] All but one of the RCTs found no significant difference in rates of clinical cure between different topical antibiotics. One RCT with methodological flaws (see comment) comparing moxifloxacin (a fourth-generation quinolone) with combination trimethoprim/polymyxin (a common first-line antibiotic) found that moxifloxacin significantly increased clinical and microbiological cure rates compared with trimethoprim/polymyxin. [40] All but three RCTs [25] [28] [40] also found no significant difference in rates of microbiological cure.

Topical versus oral antibiotics:
We found one RCT (80 children). [41] It found no significant difference in clinical improvement or bacteriological failure rates between polymyxin B sulphate–bacitracin ointment plus oral placebo versus topical placebo plus oral cefixime (see table 1, p 13). However, it may have been underpowered to detect a clinically important difference between treatments.

Different regimens of topical antibiotics versus each other:
We found one RCT. [42] The RCT (104 people with acute conjunctivitis) found no significant difference in rate of clinical cure between gatifloxacin used twice daily versus four times daily (cure rate by fifth day: 45/52 [87%] with twice-daily dosage *v* 37/52 [71%] with four-times-daily dosage; P = 0.96).

Harms:

Topical antibiotics versus placebo:
The review gave no information on adverse effects. [15] Two RCTs identified by the review found similar rates of adverse effects between topical antibiotics and placebo. [11] [19] One RCT identified by the review found that fusidic acid significantly increased adverse events compared with placebo. [20] The subsequent RCT found that one person receiving immediate antibiotics had cellulitis; it gave no further information on adverse effects (see table 1, p 13). One large population-based prospective cohort study (4.2 million people) found that topical chloramphenicol was associated with aplastic anaemia, but that the incidence was extremely low: 0.36 cases per million weeks of treatment with chloramphenicol. The incidence of aplastic anaemia was 0.04 per million weeks in people who did not take chloramphenicol. [43] One non-systematic review reported three cases of Stevens–Johnson syndrome in people using topical sulphonamides. [44] However, the review did

not report the number of people using these drugs, making it difficult to exclude other possible causes of this condition. The RCT comparing three interventions (immediate antibiotics, delayed antibiotics, or no antibiotics) reported one case of orbital cellulitis in a participant who received immediate chloramphenicol drops. [18] One non-systematic review (5 RCTs; 1978 adults and children) assessing safety found that moxifloxacin 0.5% given two to three times daily was associated with similar rates of overall adverse effects compared with vehicle ointment (4.7% with moxifloxacin *v* 2.6% with vehicle; no further data reported). [45] The most common adverse effect in both groups was ocular discomfort.

Topical antibiotics versus each other:
RCTs found different rates of adverse effects (usually mild, such as burning, stinging, irritation, and bad taste) with the different agents (see table 1, p 13). [22] [23] [24] [21] [25] [26] [27] [28] [29] [30] [31] [32] [33] [34] [35] [36] [37] [38] [39] [42] [40] Most RCTs did not assess the significance of the difference in adverse effects between groups. One non-systematic review (5 RCTs; 1978 adults and children) assessing safety found that moxifloxacin 0.5% given two to three times daily, ciprofloxacin given three times daily, or ofloxacin given four times daily were associated with similar rates of overall adverse effects (no further data about total overall adverse effects or significance assessment reported). [45] The most common adverse effect in all groups was ocular discomfort.

Topical versus oral antibiotics:
The RCT did not report on adverse effects. [41]

Different regimens of topical antibiotics versus each other:
The RCT found similar rates of adverse effects with two- and four-times-daily ciprofloxacin (10% in both groups; significance not reported). [42]

Comment:

One RCT identified by the review relied primarily on self-report of clinical cure by the parents of the paediatric participants. [19] This RCT showed re-infection (relapse or new infection) rates to be low (less than 5%) and distributed equally between chloramphenicol and placebo. [19] Most of the trials above included children as well as adults, and the ratio of children to adults was usually not specified. The comparisons of lomefloxacin versus chloramphenicol [26] and fusidic acid, [34] the comparison of norfloxacin versus fusidic acid, [24] and the comparison of tobramycin versus fusidic acid [38] were single-blinded. The comparison of moxifloxacin versus trimethoprim/polymyxin B was potentially flawed by a mismatch of the unit of randomisation (people) and the unit of analysis (eyes) as well as by the comparison of standard adult dosing of moxifloxacin to the minimum (and rarely studied) adult dose of trimethoprim/polymixin B. [40] One RCT found that a significantly greater proportion of participants rated topical tobramycin as more inconvenient than the viscous preparation of fusidic acid, because of a difference in the frequency of administration. [38] The RCT also found that adherence among children was significantly higher with fusidic acid. We found no evidence on empirical antibiotic treatment specifically in contact lens wearers. In all of the RCTs, contact lens use was either not specified or was specified as an exclusion criterion, or the use of contact lenses was prohibited during the trial. None of the RCTs analysed data separately in contact lens wearers. Using eye culture swabs to guide therapy and patient information leaflets did not affect treatment outcomes.

Clinical guide:
Because of a relatively high spontaneous remission rate, there is only a marginal benefit from antibiotics for suspected bacterial conjunctivitis. The "delayed antibiotics" approach detailed in the RCT above [18] seems to address the clinical uncertainties of the diagnosis and management of conjunctivitis most appropriately. There is no clear best choice for topical antibiotics — local microbiological resistance patterns, cost, and other patient factors (e.g., allergies, compliance) are important considerations in addition to efficacy.

OPTION EMPIRICAL TREATMENT WITH ORAL ANTIBIOTICS IN PEOPLE WITH SUSPECTED BACTERIAL CONJUNCTIVITIS

We found no direct information from RCTs about oral antibiotics in the treatment of people with suspected bacterial conjunctivitis.

For GRADE evaluation of interventions for bacterial conjunctivitis, **see table, p 21 .**

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

OPTION EMPIRICAL TREATMENT WITH OCULAR DECONGESTANTS IN PEOPLE WITH SUSPECTED BACTERIAL CONJUNCTIVITIS

We found no direct information from RCTs about ocular decongestants in the treatment of people with suspected bacterial conjunctivitis.

For GRADE evaluation of interventions for bacterial conjunctivitis, **see table, p 21 .**

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

OPTION EMPIRICAL TREATMENT WITH SALINE IN PEOPLE WITH SUSPECTED BACTERIAL CONJUNCTIVITIS

We found no direct information from RCTs about saline in the treatment of people with suspected bacterial conjunctivitis.

For GRADE evaluation of interventions for bacterial conjunctivitis, **see table, p 21 .**

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

OPTION EMPIRICAL TREATMENT WITH WARM COMPRESSES IN PEOPLE WITH SUSPECTED BACTERIAL CONJUNCTIVITIS

We found no direct information from RCTs about warm compresses in the treatment of people with suspected bacterial conjunctivitis.

For GRADE evaluation of interventions for bacterial conjunctivitis, **see table, p 21 .**

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

QUESTION What are the effects of treatment in adults and children with bacteriologically confirmed bacterial conjunctivitis?

OPTION ANTIBIOTICS (TOPICAL) IN PEOPLE WITH CULTURE-POSITIVE NON-GONOCOCCAL BACTERIAL CONJUNCTIVITIS

Cure rates

Compared with placebo Topical antibiotics (polymyxin B sulphate–bacitracin, ciprofloxacin, ofloxacin, levofloxacin, moxifloxacin, besifloxacin, and azithromycin) seem more effective than placebo at increasing clinical and microbiological cure at 2 to 10 days (moderate-quality evidence).

Compared with each other We don't know whether any one topical antibiotic is consistently more effective at improving clinical or microbiological cure (low-quality evidence).

Different regimens compared with each other We don't know whether a three-times-daily application of levofloxacin drops is more effective than a standard dosing regimen at improving clinical or microbiological cure in people aged 18 to 70 years (low-quality evidence).

For GRADE evaluation of interventions for bacterial conjunctivitis, **see table, p 21 .**

Benefits:

Topical antibiotics versus placebo:
We found one systematic review (search date 2004), [15] three subsequent RCTs, [46] [47] [48] and five additional RCTs [49] [50] [51] [52] [53] in people with culture-positive bacterial conjunctivitis, comparing antibiotics (polymyxin B sulphate–bacitracin, ciprofloxacin, ofloxacin, levofloxacin,

moxifloxacin, besifloxacin, azithromycin) versus placebo or vehicle only (see table 1, p 13). The review performed a meta-analysis including RCTs of both suspected and confirmed culture-positive bacterial conjunctivitis, but did not perform separate meta-analyses for these populations; we therefore report results of the individual RCTs here. All but one of the RCTs in people with culture-positive bacterial conjunctivitis (1933 people) found that topical antibiotics (ciprofloxacin, levofloxacin, moxifloxacin, ofloxacin, besifloxacin, azithromycin) significantly increased clinical and microbiological cure rates over 2 to 10 days compared with placebo. [47] [48] [49] [50] [51] [52] [53] The RCT (18 people), which found different results to the others in people with culture-positive bacterial conjunctivitis found that a significant increase in clinical cure at 3 to 5 days with polymyxin B sulphate plus bacitracin compared with placebo was not sustained at 8 to 10 days. [46] This RCT also found that, in a separate analysis of people already receiving systemic antibiotics for culture-positive bacterial conjunctivitis, there was no significant difference in clinical or microbiological cure at 3 to 5 days between adding polymyxin B sulphate–bacitracin and adding placebo. [46]

Topical antibiotics versus each other:
We found no systematic review but found nine RCTs in 10 reports (see table 1, p 13). [47] [54] [55] [56] [57] [58] [59] [60] [61] [62] Most RCTs found no significant difference between different topical antibiotics in clinical or microbiological cure rates. Two RCTs found no significant difference in cure rates between ciprofloxacin and tobramycin after 7 days; one assessed both clinical and microbiological cure rates, [55] and the other assessed reduction or eradication of bacteria. [47] A third RCT found that topical fusidic acid significantly increased clinical cure rate compared with chloramphenicol. [54] The fourth and fifth RCTs comparing topical levofloxacin versus ofloxacin found inconclusive results. [59] [60] The fourth RCT found that topical levofloxacin for 5 days significantly increased microbiological cure rate compared with topical ofloxacin, but found no significant difference in clinical cure rate at 6 to 10 days. [59] The fifth RCT found similar clinical improvement rates, and no significant difference in time until improvement, between levofloxacin and ofloxacin. [60] The sixth RCT found no significant difference in symptom resolution after 7 days between lomefloxacin and ofloxacin. [57] The seventh RCT found that topical netilmicin significantly increased clinical cure rate after both 5 and 10 days compared with topical gentamicin. [58] The eighth RCT compared three topical antibiotics: trimethoprim–polymyxin B sulphate, gentamicin, and sulfacetamide (sulphacetamide). [56] It found no significant difference between antibiotics in clinical or microbiological cure rates after 2 to 7 days. The ninth RCT (results reported in 2 papers) compared azithromycin versus tobramycin in a non-inferiority study and found no significant differences in microbiological or clinical cure rates at 9 days. [61] [62]

Different regimens of topical antibiotics versus each other:
We found one single-blinded RCT comparing levofloxacin 0.5% drops given one drop three times daily versus "standard dosing" (1 drop every 2 hours for 2 days, then 1 drop every 6 hours for 5 days) in adults. [63] The study found no difference in microbiological or clinical cure rates (see table 1, p 13). [63]

Harms:

Topical antibiotics versus placebo:
The RCTs found minimal and infrequent adverse effects, with no significant differences between topical antibiotics and placebo (see table 1, p 13). [46] [47] [48] [49] [50]

Topical antibiotics versus each other:
The RCTs found infrequent adverse effects with the different topical antibiotics, with no significant differences between the different topical antibiotics reported (see table 1, p 13). [47] [54] [55] [56] [57] [58] [59] [60] The harms of the different topical antibiotics are unlikely to differ between people with suspected and culture-confirmed bacterial conjunctivitis (see also harms of topical antibiotics in people with suspected bacterial conjunctivitis, p 6).

Different regimens of topical antibiotics versus each other:
The RCT found no difference in rates of adverse effects between the two study dosing regimens for levofloxacin. [63]

Comment:

None of the RCTs addressed the effect on antibiotic resistance of using topical antibiotics in bacterial conjunctivitis, which would be of interest given the self-limiting nature of the disease. The ages of the people in the studies were not always specified. In most of the RCTs, people were randomised and began treatment before their culture results were available, and people with negative baseline culture results were excluded from the efficacy analyses. Therefore, these results may not be generalisable to situations where treatment is not initiated until culture results are known, because of the delay in treatment. We found no studies that examined this option. The harms data for topical antibiotics versus each other are not specific to culture-positive patients. [59] [60] [22] [23] [24] We found no evidence on antibiotics specifically in contact lens wearers with culture-positive bacterial conjunctivitis. Reviewing all of the RCTs, contact lens use was either not specified or specified as an exclusion criterion, or the use of contact lenses was prohibited during the trial.

None of the RCTs analysed data separately in contact lens wearers. The study of different dosing regimens of levofloxacin was not blinded to the subjects, but this did not appear to result in a significant placebo effect. [63]

Clinical guide:
Antibiotics for confirmed bacterial conjunctivitis lead to slightly higher clinical cure rates than placebo, but there remains a high spontaneous cure rate. There is no clear best choice for topical antibiotics — local microbiological resistance patterns, cost, dosing regimens, and other patient factors (such as allergies and compliance) are important considerations in addition to efficacy.

OPTION OCULAR DECONGESTANTS IN PEOPLE WITH CONFIRMED BACTERIAL CONJUNCTIVITIS

We found no direct information from RCTs about ocular decongestants in the treatment of people with confirmed bacterial conjunctivitis.

For GRADE evaluation of interventions for bacterial conjunctivitis, see table, p 21 .

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

OPTION SALINE IN PEOPLE WITH CONFIRMED BACTERIAL CONJUNCTIVITIS

We found no direct information from RCTs about saline in the treatment of treatment of people with confirmed bacterial conjunctivitis.

For GRADE evaluation of interventions for bacterial conjunctivitis, see table, p 21 .

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

OPTION WARM COMPRESSES IN PEOPLE WITH CONFIRMED BACTERIAL CONJUNCTIVITIS

We found no direct information from RCTs about warm compresses in the treatment of people with confirmed bacterial conjunctivitis.

For GRADE evaluation of interventions for bacterial conjunctivitis, see table, p 21 .

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

QUESTION What are the effects of treatment in adults and children with clinically confirmed gonococcal conjunctivitis?

OPTION ANTIBIOTICS (PARENTERAL OR TOPICAL) IN PEOPLE WITH SUSPECTED OR CONFIRMED GONOCOCCAL CONJUNCTIVITIS

Cure rates
Parenteral plus topical antibiotic compared with parenteral antibiotic alone or parenteral plus different topical antibiotic We don't know whether parenteral plus topical antibiotic is more effective than parenteral antibiotic alone at increasing clinical or microbiological cure rates in neonates with gonococcal conjunctivitis in Africa. We don't know whether parenteral kanamycin plus topical gentamicin is more effective than parenteral kanamycin plus topical chloramphenicol at improving cure rates in neonates with gonococcal conjunctivitis in Africa. We found no RCTs performed outside Africa (very low-quality evidence).

Note
There is consensus that single-dose parenteral antibiotics followed by topical antibiotics at the clinician's discretion are likely to be beneficial in people with suspected or confirmed gonococcal conjunctivitis.

For GRADE evaluation of interventions for bacterial conjunctivitis, see table, p 21 .

Benefits: We found no systematic reviews but found four RCTs, three reported in one paper. [64] [65] All RCTs were carried out by the same research group treating gonococcal ophthalmia neonatorum in Africa. The first RCT (122 neonates with gonococcal conjunctivitis) compared three interventions: single-dose parenteral ceftriaxone 125 mg alone; single-dose parenteral kanamycin 75 mg plus topical gentamicin for 7 days; and single-dose parenteral kanamycin 75 mg plus topical tetracycline for 7 days. [65] The RCT found no significant difference between groups in rates of persistent or recurrent gonococcal conjunctivitis over 14 days (0/61 [0%] with ceftriaxone *v* 2/32 [6%] with kanamycin/gentamicin *v* 1/29 [3%] with kanamycin/tetracycline; reported as not significant; P value not reported). The other three RCTs (117 neonates with gonococcal conjunctivitis) were all reported in one paper. [64] The first RCT (53 neonates) compared parenteral kanamycin 75 mg plus topical gentamicin for 3 days versus parenteral kanamycin 75 mg plus saline washes for 3 days. [64] It found that single-dose parenteral kanamycin 75 mg plus topical gentamicin significantly improved bacteriological cure rate at 30 days compared with single-dose parenteral kanamycin 75 mg alone (cure rate: 87% with kanamycin/gentamicin *v* 60% with kanamycin/saline washes; P = 0.03). The second RCT (38 infants) compared single-dose parenteral kanamycin 150 mg plus topical gentamicin for 3 days versus parenteral kanamycin 150 mg plus saline washes for 3 days. It found no significant difference in bacteriological cure rate between single-dose parenteral kanamycin 150 mg plus topical gentamicin for 3 days versus single-dose parenteral kanamycin 150 mg alone (cure rate: 87% with kanamycin/gentamicin *v* 89.5% with kanamycin/saline washes; reported as not significant; P value not reported). The third RCT (26 infants) compared parenteral kanamycin 150 mg plus topical gentamicin versus parenteral kanamycin 150 mg plus topical chloramphenicol. It stated that parenteral kanamycin 150 mg plus topical chloramphenicol resulted in cure rates of 80% — similar to those reported for parenteral kanamycin (150 mg) plus topical gentamicin (86%) — but did not directly assess the difference between groups.

Harms: The RCTs gave no information on adverse effects. [64] [65]

Comment: **Clinical guide:** In many hospital settings, antibiotic prophylaxis against gonococcal conjunctivitis — with silver nitrate or with antibacterial ointment — is part of routine care of the neonate. [3] There is consensus that parenteral antibiotics are likely to be beneficial in people with suspected or confirmed gonococcal conjunctivitis. The management of gonococcal ophthalmia neonatorum is directed by guidelines based apparently in part on the trials described above. [64] [65] Ceftriaxone is recommended for parenteral treatment, followed by ointment or saline washes at the clinician's discretion. There is no evidence from developed countries to guide therapy beyond these guidelines. Neonates will usually require investigation for concomitant infections and complications.

OPTION ANTIBIOTICS (ORAL) IN PEOPLE WITH SUSPECTED OR CONFIRMED GONOCOCCAL CONJUNCTIVITIS

We found no direct information from RCTs about oral antibiotics alone in the treatment of people with suspected or confirmed gonococcal conjunctivitis.

For GRADE evaluation of interventions for bacterial conjunctivitis, see table, p 21 .

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

OPTION OCULAR DECONGESTANTS IN PEOPLE WITH SUSPECTED OR CONFIRMED GONOCOCCAL CONJUNCTIVITIS

We found no direct information from RCTs about ocular decongestants in the treatment of people with suspected or confirmed gonococcal conjunctivitis.

For GRADE evaluation of interventions for bacterial conjunctivitis, see table, p 21 .

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

OPTION SALINE IN PEOPLE WITH SUSPECTED OR CONFIRMED GONOCOCCAL CONJUNCTIVITIS

We found no direct information from RCTs about saline in the treatment of people with suspected or confirmed gonococcal conjunctivitis.

For GRADE evaluation of interventions for bacterial conjunctivitis, **see table, p 21 .**

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

OPTION WARM COMPRESSES IN PEOPLE WITH SUSPECTED OR CONFIRMED GONOCOCCAL CONJUNCTIVITIS

We found no direct information from RCTs about warm compresses in the treatment of people with suspected or confirmed gonococcal conjunctivitis.

For GRADE evaluation of interventions for bacterial conjunctivitis, **see table, p 21 .**

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

GLOSSARY

Low-quality evidence Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Moderate-quality evidence Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Very low-quality evidence Any estimate of effect is very uncertain.

SUBSTANTIVE CHANGES

Antibiotics (topical) in people with culture-positive non-gonococcal bacterial conjunctivitis Five RCTs added. [51] [52] [53] [61] [63] The first three RCTs compared topical antibiotics versus placebo and found that topical antibiotics (ciprofloxacin, levofloxacin, moxifloxacin, ofloxacin, besifloxacin, azithromycin) increased clinical and microbiological cure rates over 2 to 10 days compared with placebo. [51] [52] [53] The fourth RCT compared topical antibiotics versus each other and found no significant difference between groups in microbiological or clinical cure rates at 9 days. [61] The fifth RCT compared levofloxacin 0.5% drops given one drop three times daily versus "standard dosing" (1 drop every 2 hours for 2 days, then 1 drop every 6 hours for 5 days) in adults, and found no significant difference in microbiological or clinical cure rates with different dose frequencies. [63] Categorisation unchanged (Beneficial).

Empirical treatment with topical antibiotics in people with suspected bacterial conjunctivitis One RCT with weak methods added comparing moxifloxacin versus combination trimethoprim/polymyxin. [40] The RCT found that moxifloxacin increased clinical and microbiological cure rates compared with trimethoprim/polymyxin, which ran contrary to findings of multiple other RCTs that found equivalent effectiveness for these outcomes when different antibiotics were compared with each other. Categorisation unchanged (Likely to be beneficial).

REFERENCES

1. Limberg, MB. A review of bacterial keratitis and bacterial conjunctivitis. *Am J Ophthalmology* 1991;112:2S–9S.
2. Thadani SM, Foster CS. Treatment of ocular inflammation in children. *Pediatr Drugs* 2004;6:289–301.
3. Woods CR. Gonococcal infections in neonates and young children. *Semin Pediatr Infect Dis* 2005;16:258–270.[PubMed]
4. Rietveld RP, Weert H, Bindels PJE. Diagnostic impact of signs and symptoms in acute infectious conjunctivitis: systematic literature search. *BMJ* 2003;327:789.[PubMed]
5. Rietveld RP, ter Riet G, Bindels PJ, et al. Predicting bacterial cause in infectious conjunctivitis: cohort study on informativeness of combinations of signs and symptoms. *BMJ* 2004;329:206–208.[PubMed]
6. McLeod SD. Infectious keratitis. In: Yanoff M, Duker JS, eds. *Ophthalmology*, 2nd ed. St. Louis, MO: Mosby, Inc., 2004.
7. Wishart PK, James C, Wishart MS, et al. Prevalence of acute conjunctivitis caused by chlamydia, adenovirus, and herpes simplex virus in an ophthalmic casualty department. *Br J Ophthalmol* 1984;68:653–655.[PubMed]
8. Fitch CP, Rapoza PA, Owens S, et al. Epidemiology and diagnosis of acute conjunctivitis at an inner-city hospital. *Ophthalmology* 1989;96:1215–1220.[PubMed]
9. Woodland RM, Darougar S, Thaker U, et al. Causes of conjunctivitis and keratoconjunctivitis in Karachi, Pakistan. *Trans R Soc Trop Med Hygiene* 1992;86:317–320.
10. Seal DV, Barrett SP, McGill JI. Aetiology and treatment of acute bacterial infection of the external eye. *Br J Ophthalmol* 1982;66:357–360.
11. Miller IM, Wittreich J, Vogel R, et al, for the Norfloxacin-Placebo Ocular Study Group. The safety and efficacy of topical norfloxacin compared with placebo in the treatment of acute bacterial conjunctivitis. *Eur J Ophthalmol* 1992;2:58–66.[PubMed]
12. Gigliotti F, Williams WT, Hayden FG, et al. Etiology of acute conjunctivitis in children. *J Pediatr* 1981;98:531–536.[PubMed]
13. Weiss A, Brinser JH, Nazar-Stewart V. Acute conjunctivitis in childhood. *J Pediatr* 1993;122:10–14.[PubMed]
14. Buznach N, Dagan R, Greenberg D. Clinical and bacterial characteristics of acute bacterial conjunctivitis in children in the antibiotic resistance era. *Pediatr Infect Dis J* 2005;24:823–828.[PubMed]

15. Sheikh A, Hurwitz B. Topical antibiotics for acute bacterial conjunctivitis: Cochrane systematic review and meta-analysis update. *Br J Gen Pract* 2005;55:962–964.[PubMed]
16. Bodor FF. Conjunctivitis–otitis media syndrome: more than meets the eye. *Contemp Pediatr* 1989;6:55–60.
17. Barquet N, Gasser I, Domingo P, et al. Primary meningococcal conjunctivitis: report of 21 patients and review. *Rev Infect Dis* 1990;12:838–847.[PubMed]
18. Everitt HA, Little PS, Smith PWF. A randomised controlled trial of management strategies for acute infective conjunctivitis in general practice. *BMJ* 2006;333:321–324.[PubMed]
19. Rose PW, Harnden A, Brueggemann AB, et al. Chloramphenicol treatment for acute infective conjunctivitis in children in primary care: a randomised, double-blind, placebo controlled trial. *Lancet* 2005;366:37–42.
20. Rietveld RP, ter Riet G, Bindels PJE et al. The treatment of acute infectious conjunctivitis with fusidic acid: a randomised trial. *Br J Gen Pract* 2005;55:924–930.[PubMed]
21. The Trimethoprim–Polymyxin B Sulphate Ophthalmic Ointment Study Group. Trimethoprim–polymyxin B sulphate ophthalmic ointment versus chloramphenicol ophthalmic ointment in the treatment of bacterial conjunctivitis — a review of four clinical studies. *J Antimicrob Chemother* 1989;23:261–266.[PubMed]
22. Montero J, Casado A, Perea E, et al. A double-blind double-dummy comparison of topical lomefloxacin 0.3% twice daily with topical gentamicin 0.3% four times daily in the treatment of acute bacterial conjunctivitis. *J Clin Res* 1998;1:29–39.
23. Alves MR, Kara JN. Evaluation of the clinical and microbiological efficacy of 0.3% ciprofloxacin drops and 0.3% tobramycin drops in the treatment of acute bacterial conjunctivitis. *Rev Bras Oftalmol* 1993;52:371–377.
24. Wall AR, Sinclair N, Adenis JP. Comparison of Fucithalmic (fusidic acid viscous eye drops 1%) and Noroxin (norfloxacin ophthalmic solution 0.3%) in the treatment of acute bacterial conjunctivitis. *J Clin Res* 1998;1:316–325.
25. Kettenmeyer A, Jauch A, Boscher M, et al. A double-blind double-dummy multicenter equivalence study comparing topical lomefloxacin 0.3% twice daily with norfloxacin 0.3% four times daily in the treatment of acute bacterial conjunctivitis. *J Clin Res* 1998;1:75–86.
26. Agius-Fernandez A, Patterson A, Fsadni M, et al. Topical lomefloxacin versus topical chloramphenicol in the treatment of acute bacterial conjunctivitis. *Clin Drug Invest* 1998;15:263–269.
27. Adenis JP, Arrata M, Gastaud P, et al. A multicenter randomized study of fusidic acid ophthalmic gel and rifamycin eyedrops in acute conjunctivitis. *J Fr Ophtalmol* 1989;12:317–322. [In French.][PubMed]
28. Huerva V, Ascaso FJ, Latre B, et al. Tolerancia y eficacia de la tobramicina topica vs cloranfenicol en el tratamiento de las conjunctivitis bacterianas. *Ciencia Pharmaceutica* 1991;1:221–224.
29. Gallenga PE, Lobefalo L, Colangelo L, et al. Topical lomefloxacin 0.3% twice daily versus tobramycin 0.3% in acute bacterial conjunctivitis: a multicenter double-blind phase III study. *Ophthalmologica* 1999;213:250–257.[PubMed]
30. Behrens-Baumann W, Quentin CD, Gibson JR, et al. Trimethoprim–polymyxin B sulphate ophthalmic ointment in the treatment of bacterial conjunctivitis: a double-blind study versus chloramphenicol ophthalmic ointment. *Curr Med Res Opin* 1988;11:227–231.[PubMed]
31. Van-Rensburg SF, Gibson JR, Harvey SG, et al. Trimethoprim–polymyxin ophthalmic solution versus chloramphenicol ophthalmic solution in the treatment of bacterial conjunctivitis. *Pharmatherapeutica* 1982;3:274–277.[PubMed]
32. Gibson JR. Trimethoprim–polymyxin B ophthalmic solution in the treatment of presumptive bacterial conjunctivitis — a multicentre trial of its efficacy versus neomycin–polymyxin B–gramicidin and chloramphenicol ophthalmic solutions. *J Antimicrob Chemother* 1983;11:217–221.
33. Genee E, Schlechtweg C, Bauerreiss P, et al. Trimethoprim–polymyxin eye drops versus neomycin–polymyxin–gramicidin eye drops in the treatment of presumptive bacterial conjunctivitis — a double-blind study. *Ophthalmologica* 1982;184:92–96.[PubMed]
34. Malminiemi K, Kari O, Latvala M-L, et al. Topical lomefloxacin twice daily compared with fusidic acid in acute bacterial conjunctivitis. *Acta Ophthalmol Scand* 1996;74:280–284.
35. Carr WD. Comparison of Fucithalmic (fusidic acid viscous eye drops 1%) and Chloromycetin Redidrops (chloramphenicol eye drops 0.5%) in the treatment of acute bacterial conjunctivitis. *J Clin Res* 1998;1:403–411.
36. Horven I. Acute conjunctivitis. A comparison of fusidic acid viscous eye drops and chloramphenicol. *Acta Ophthalmol* 1993;71:165–168.
37. Hvidberg J. Fusidic acid in acute conjunctivitis. Single-blind, randomized comparison of fusidic acid and chloramphenicol viscous eye drops. *Acta Ophthalmol* 1987;65:43–47.
38. Jackson WB, Low DE, Dattani D, et al. Treatment of acute bacterial conjunctivitis: 1% fusidic acid viscous drops vs. 0.3% tobramycin drops. *Can J Ophthalmol* 2002;37:228–237.
39. Sinclair NM, Leigh DA. A comparison of fusidic acid viscous eye drops and chloramphenicol eye ointment in acute conjunctivitis. *Curr Ther Res* 1988;44:468–474.
40. Granet DB, Dorfman M, Stroman D, et al. A multicenter comparison of polymyxin B sulfate/trimethoprim ophthalmic solution and moxifloxacin in the speed of clinical efficacy for the treatment of bacterial conjunctivitis. *J Pediatr Ophthalmol Strabismus* 2008;45:340–349.[PubMed]
41. Wald ER, Greenberg D, Hoberman A. Short term oral cefixime therapy for treatment of bacterial conjunctivitis. *Pediatr Infect Dis J* 2001;20:1039–1042.[PubMed]
42. Yee R, Jensen H. A clinical comparison of the efficacy and safety of gatifloxacin 0.3% Administered bid or qid for the treatment of acute bacterial conjunctivitis. American Academy of Optometry; 2004. Available at http://www.aaopt.org/Submission/Search/SubmissionViewer.asp?SID=5479&BR=SP (last accessed 12 February 2010).
43. Laporte JR, Vidal X, Ballarin E, et al. Possible association between ocular chloramphenicol and aplastic anaemia - the absolute risk is very low. *Br J Clin Pharmacol* 1998;46:181–184.[PubMed]
44. Stern GA, Killingsworth DW. Complications of topical antimicrobial agents. *Int Ophthalmol Clin* 1989;29:137–142.
45. Silver LH, Woodside AM, Montgomery DB. Clinical safety of moxifloxacin ophthalmic solution 0.5% (VIGAMOX) in pediatric and nonpediatric patients with bacterial conjunctivitis. *Surv Ophthalmol* 2005;50(Suppl 1):S55–S63.[PubMed]
46. Gigliotti G, Hendley JO, Morgan J, et al. Efficacy of topical antibiotic therapy in acute conjunctivitis in children. *J Pediatr* 1984;104:623–626.[PubMed]
47. Leibowitz HM. Antibacterial effectiveness of ciprofloxacin 0.3% ophthalmic solution in the treatment of bacterial conjunctivitis. *Am J Ophthalmol* 1991;112:29S–33S.
48. Ofloxacin Study Group III. A placebo-controlled clinical study of the fluoroquinolone ofloxacin in patients with external infection. *Invest Ophthalmol Vis Sci* 1990;31:572.
49. Hwang DG, Schanzlin DJ, Rotberg MH, et al. A phase III, placebo controlled clinical trial of 0.5% levofloxacin ophthalmic solution for the treatment of bacterial conjunctivitis. *Br J Ophthalmol* 2003;87:1004–1009.[PubMed]
50. Gross RD, Lichtenstein SJ, Schlech BA. Early clinical and microbiological responses in the treatment of bacterial conjunctivitis with moxifloxacin ophthalmic solution 0.5% (vigamox) using BID dosing. *Todays Ther Trends* 2003;21:227–237.
51. Karpecki P, Depaolis M, Hunter JA, et al. Besifloxacin ophthalmic suspension 0.6% in patients with bacterial conjunctivitis: a multicenter, prospective, randomized, double-masked, vehicle-controlled, 5-day efficacy and safety study. *Clin Ther* 2009;31:514–526.[PubMed]
52. Tepedino ME, Heller WH, Usner DW, et al. Phase III efficacy and safety study of besifloxacin ophthalmic suspension 0.6% in the treatment of bacterial conjunctivitis. *Curr Med Res Opin* 2009;25:1159–1169.[PubMed]
53. Abelson MB, Heller W, Shapiro AM, et al. Clinical cure of bacterial conjunctivitis with azithromycin 1%: vehicle-controlled, double-masked clinical trial. *Am J Ophthalmol* 2008;145:959–965.[PubMed]
54. Van Bijsterveld OP, El Batawi Y, Sobhi FS, et al. Fusidic acid in infections of the external eye. *Infection* 1987;15:16–19.[PubMed]
55. Gross RD, Hoffman RO, Lindsay RN. A comparison of ciprofloxacin and tobramycin in bacterial conjunctivitis is children. *Clin Pediatr* 1997;36:435–444.
56. Lohr JA, Austin RD, Grossman M, et al. Comparison of three topical antimicrobials for acute bacterial conjunctivitis. *Pediatr Infect Dis J* 1988;7:626–629.[PubMed]
57. Tabbara KF, El-Sheik HF, Monowarul Islam SM, et al. Treatment of acute bacterial conjunctivitis with topical lomefloxacin 0.3% compared to topical ofloxacin 0.3%. *Eur J Ophthalmol* 1999;9:269–275.[PubMed]
58. Papa V, Aragona P, Scuderi AC, et al. Treatment of acute bacterial conjunctivitis with topical netilmicin. *Cornea* 2002;21:43–47.[PubMed]
59. Schwab IR, Friedlaender M, McCulley J, et al, and the Levofloxacin Bacterial Conjunctivitis Active Control Study Group. A phase III clinical trial of 0.5% levofloxacin ophthalmic solution versus 0.3% ofloxacin ophthalmic solution for the treatment of bacterial conjunctivitis. *Ophthalmology* 2003;110:457–465.[PubMed]
60. Zhang M, Hu Y, Chen F. Clinical investigation of 0.3% levofloxacin eyedrops on the treatment of cases with acute bacterial conjunctivitis and bacterial keratitis. *Yen ko Hsueh Pao [Eye Science]* 2000;16:146–148.
61. Denis F, Chaumeil C, Goldschmidt P, et al. Microbiological efficacy of 3-day treatment with azithromycin 1.5% eyedrops for purulent bacterial conjunctivitis. *Eur J Ophthalmol* 2008;18:858–868.[PubMed]
62. Cochereau I, Meddeb-Ouertani A, Khairallah M, et al. 3-day treatment with azithromycin 1.5% eye drops versus 7-day treatment with tobramycin 0.3% for purulent bacterial conjunctivitis: multicentre, randomised and controlled trial in adults and children. *Br J Ophthalmol* 2007;91:465–469.[PubMed]
63. Szaflik J, Szaflik JP, Kaminska A, et al. Clinical and microbiological efficacy of levofloxacin administered three times a day for the treatment of bacterial conjunctivitis. *Eur J Ophthalmol* 2009;19:1–9.[PubMed]
64. Fransen L, Nsanze H, D'Costa L, et al. Single-dose kanamycin therapy of gonococcal ophthalmia neonatorum. *Lancet.* 1984;2:1234–1237.[PubMed]
65. Laga M, Naamara W, Brunham RC, et al. Single-dose therapy of gonococcal ophthalmia neonatorum with ceftriaxone. *N Engl J Med* 1986;315:1382–1385.[PubMed]

John Epling
Associate Professor
Department of Family Medicine
State University of New York-Upstate Medical University
Syracuse, New York
USA

Competing interests: JE declares that he has no competing interests.

Disclaimer

The information contained in this publication is intended for medical professionals. Categories presented in Clinical Evidence indicate a judgement about the strength of the evidence available to our contributors prior to publication and the relevant importance of benefit and harms. We rely on our contributors to confirm the accuracy of the information presented and to adhere to describe accepted practices. Readers should be aware that professionals in the field may have different opinions. Because of this and regular advances in medical research we strongly recommend that readers' independently verify specified treatments and drugs including manufacturers' guidance. Also, the categories do not indicate whether a particular treatment is generally appropriate or whether it is suitable for a particular individual. Ultimately it is the readers' responsibility to make their own professional judgements, so to appropriately advise and treat their patients. To the fullest extent permitted by law, BMJ Publishing Group Limited and its editors are not responsible for any losses, injury or damage caused to any person or property (including under contract, by negligence, products liability or otherwise) whether they be direct or indirect, special, incidental or consequential, resulting from the application of the information in this publication.

TABLE 1 Topical antibiotics in adults and children with suspected or confirmed bacterial conjunctivitis: results of RCTs

Intervention	Number of participants	Age of participants	Proportion culture-positive	Microbiological cure rate	Clinical cure rate	Adverse effects
Topical antibiotics versus placebo						
Suspected bacterial conjunctivitis						
Norfloxacin 0.3% every 2 hours while awake, for 1 day, then 4 times daily for 5–6 more days [11]	284 adults	18 years and over	With or without positive cultures	At 2–3 days: 65% with norfloxacin *v* 26% with placebo; P less than 0.01 At 5–7 days (excluding coagulase-negative *Staphylococcus*): 74% with norfloxacin *v* 42% with placebo; P less than 0.01	At 5 days: 88% with norfloxacin *v* 72% with placebo; P less than 0.01	Minor events (including chemosis and burning): 4% with norfloxacin *v* 7% with placebo; significance not reported
Chloramphenicol 0.5% 1 drop every 2 hours while awake, for 1 day, then 4 times daily until 48 hours after infection has resolved [19]	326 children	6 months–12 years	78%	Microbiological cure: 40% with chloramphenicol *v* 23% with placebo at 7 days; ARI 17%, 95% CI 5.5% to 28.1% Microbiological cure or improvement at 7 days: 65% with chloramphenicol *v* 55% with placebo; ARI +9.6%, 95% CI –2.5% to +21.7%	At 3 days: 39% with chloramphenicol *v* 33% with placebo; ARI +6.2%, 95% CI –4.3% to +16.5% At 7 days: 86% with chloramphenicol *v* 79% with placebo; ARI +7.4%, 95% CI –0.9% to +15.6%	2% with chloramphenicol *v* 2% with placebo; ARI 0%, 95% CI –2.9% to +2.9%
Fusidic acid gel 10 mg/g 1 drop 4 times daily until 1 day after signs and symptoms disappear [20]	181 adults	18 years and over	34%	At 7 days: 76% with fusidic acid *v* 41% with placebo; ARI 34.8%, 95% CI 9.3% to 60.4%	At 7 days: 62% with fusidic acid *v* 59% with placebo; ARI +2.8, 95% CI –13.5 to +18.6	14% with fusidic acid *v* 3% with placebo; ARI 10.4%, 95% CI 1.6% to 19.1%
Chloramphenicol eye drops (immediate, every 2 hours for 2 days, then 4 times daily), chloramphenicol eye drops (delayed, same regimen, prescriptions available from surgery up to 3 days after consultation at patient's/parent's discretion), no antibiotics [18]	307 adults and children	Over 1 year, mean age 27 years	50%	Not reported	Mean symptom score (days 1–3 after consultation): 1.9 with immediate antibiotics *v* 2.1 with no antibiotics; P = 0.2 Mean symptom score (days 1–3 after consultation): 2.0 with delayed antibiotics *v* 2.1 with no antibiotics; P = 0.4	1 person in immediate-antibiotic group was admitted 11 days post-consultation for orbital cellulitis
Confirmed bacterial conjunctivitis						
Levofloxacin 0.5% [49]	249 recruited; 117 people included in efficacy analysis	2–91 years	117 culture-positive and included in per protocol cohort	At "end point", defined as the last evaluable observation (up to day 10 post-treatment): 90% with levofloxacin *v* 53% with placebo; P less than 0.001	At "end point", defined as the last evaluable observation (up to day 10 post-treatment): 77% with levofloxacin *v* 60% with placebo; P = 0.026	No significant difference between levofloxacin and placebo transient burning (2.4% of 124 people); transiently decreased vision (2.4% of 124 people) with levofloxacin

Intervention	Number of participants	Age of participants	Proportion culture-positive	Microbiological cure rate	Clinical cure rate	Adverse effects
Moxifloxacin [50]	73 recruited. Number included in efficacy analysis not reported; unclear whether analysis was restricted only to people with culture-positive bacterial conjunctivitis	1–89 years	51 culture-positive	After about 1 week of treatment: 78% with moxifloxacin *v* 39% with placebo; P = 0.005	After about 1 week of treatment: 93% with moxifloxacin *v* 63% with placebo; P = 0.009	All adverse events reported as not serious
Polymyxin B sulphate 10,000 U/g plus bacitracin 500 U/g (in ointment) 4 times daily for 7 days [46]	66	1 month–18 years	Cultures positive for *Haemophilus influenzae* or *Streptococcus pneumoniae*	Eradicated at 3–5 days: 71% with polymyxin B sulphate–bacitracin *v* 19% with placebo; P less than 0.001 Eradicated at 8–10 days: 79% with polymyxin B sulphate–bacitracin *v* 31% with placebo; P less than 0.001	Cured at 3–5 days: 62% with polymyxin B sulphate–bacitracin *v* 28% with placebo; P less than 0.02 At 8–10 days: 91% with polymyxin B sulphate–bacitracin *v* 72% with placebo cured; P greater than 0.05; NS	Allergic reaction to topical polymyxin B sulphate–bacitracin in initial group of participants
Polymyxin B sulphate plus bacitracin in people taking systemic antibiotics: amoxicillin, trimethoprim–sulfamethoxazole, cefaclor, or penicillin (subgroup analysis of RCT described above) [46]	18	1 month–18 years	Cultures positive for *H influenzae* or *S pneumoniae*	72% with polymyxin B sulphate–bacitracin eradicated at 3–5 days, and 78% at 8–10 days. In people receiving systemic antibiotics, no significant difference in microbiological cure between adding polymyxin B sulphate–bacitracin and adding placebo (reported as NS; P value not reported)	83% cured at 3–5 days; 100% cured at 8–10 days. In people receiving systemic antibiotics, there was no significant difference in clinical cure between adding polymyxin B sulphate–bacitracin and adding placebo (reported as NS; P value not reported)	Allergic reaction to topical polymyxin B sulphate–bacitracin in initial group of participants
Ciprofloxacin 0.3% every 2 hours while awake on days 0–1, then every 4 hours while awake for 1–2 more days [47]	177	Age not specified	Culture-positive	Eradicated or reduced at 3 days: 132/140 (94%) with ciprofloxacin *v* 22/37 (59%) with placebo; RR 1.59; P less than 0.001	Not reported	Adverse effects not assessed in the RCT
Ofloxacin 0.3% 6 times daily for 2 days [48]	132	Age not specified	Culture-positive	At 2 days: 72% with ofloxacin *v* 35% with placebo; P less than 0.001	Improved at 2 days: 64% with ofloxacin *v* 22% with placebo; P less than 0.001	Adverse effects not assessed in the RCT
Besifloxacin 0.6% *v* vehicle only (placebo) 1 drop 3 times daily for 5 days [51]	118 (269 in "safety" population who got drug for clinical diagnosis)	1–92 years	44%	At day 4: 90% with besifloxacin *v* 47% with vehicle; P less than 0.001 At day 8: 88.3% with besifloxacin *v* 60.3% with vehicle; P less than 0.001	At day 4: 33% with besifloxacin *v* 17.2% with vehicle; P = NS At day 8: 73.35 with besifloxacin *v* 43.1% with vehicle; P less than 0.001	Mild–moderate severity adverse events common (50% with besifloxacin *v* 53% with vehicle); 1 preseptal cellulitis in vehicle group thought unrelated to study

Intervention	Number of participants	Age of participants	Proportion culture-positive	Microbiological cure rate	Clinical cure rate	Adverse effects
Besifloxacin 0.6% *v* vehicle only (placebo) 1 drop 3 times daily for 5 days. [52]	390 culture-positive for efficacy analysis (957 enrolled for clinical diagnosis analysed for safety)	10 months–98 years	41%	At day 5: 92% with besifloxacin *v* 59% with vehicle; P less than 0.0001 At days 8–9: 88% with besifloxacin *v* 72% with vehicle; P less than 0.0001	At day 5: 45% with besifloxacin *v* 33% with vehicle; P = 0.0084 At days 8–9: 84% with besifloxacin *v* 69% with vehicle; P = 0.0011	More conjunctivitis (non-specific and bacterial) in vehicle-only group (14% with besifloxacin *v* 9% with placebo; P = 0.0047). More pruritus in besifloxacin group (1% with besifloxacin *v* 0.3% with placebo; P = 0.03) and viral conjunctivitis (0.7% with besifloxacin *v* 0% with placebo; P = 0.02)
Azithromycin 1% 1 drop twice daily on days 1 and 2, then once daily on days 3–5 *v* vehicle-only placebo dosed in same manner. [53]	685 enrolled, 630 completed, 279 analysed in per protocol analysis.	1–96 years	41%	At visit 3 (day 6 or 7): 89% with azithromycin *v* 66% with vehicle; P less than 0.001; difference, 22.0%, 95% CI 12.7% to 31.4%	At visit 3: 63.1% with azithromycin *v* 49.7% with vehicle; P less than 0.03; difference, 13.4%, 95% CI 1.9% to 25.0%	Similar between groups in frequency and magnitude
Topical antibiotics versus each other						
Suspected bacterial conjunctivitis						
Chloramphenicol 0.5% drops *v* tobramycin 0.3% [28]	50	8–81 years	36% culture-positive for bacteria (2% positive for *Candida*)	Not reported	No significant difference between chloramphenicol and tobramycin in clinical scores assessed by patients or investigators (P greater than 0.05)	0% with chloramphenicol *v* 8% with tobramycin had irritation; statistical analysis not reported
Ciprofloxacin 0.3% drops *v* tobramycin 0.3% drops; regimen unspecified (abstract reviewed, but full paper unavailable) [23]	40	Age unspecified	Not all culture-proved	80% eradication with ciprofloxacin *v* 95% with tobramycin; reported as NS	95% cure with ciprofloxacin *v* 95% with tobramycin; reported as NS	Adverse events (burning, bitter taste, pruritus, punctate epithelial erosions: 20% with ciprofloxacin *v* 35% with tobramycin
Fusidic acid 1% viscous drops twice daily *v* rifamycin 1% drops 4 times daily [27]	163	Adults and children	72%–75% culture-positive	Not reported in each group separately	Cure: 87% with fusidic acid *v* 89% with rifamycin; P = 0.71; median: 7 days with fusidic acid *v* 6 days with rifamycin; P = 0.31	Burning and bad taste: 4/74 (5%) with fusidic acid *v* 13/77 (17%) with rifamycin; reports of allergy with rifamycin
Fusidic acid 1% viscous drops twice daily *v* norfloxacin 0.3% drops 4 times daily [24]	400	Over 1 year	34% culture-positive	Not reported	Success of treatment as assessed by investigator after 7 days treatment: 91% with fusidic acid *v* 93% with norfloxacin; P = 0.49	6% with fusidic acid *v* 20% reported bad taste; P = 0.001; 37% with fusidic acid *v* 50% with norfloxacin reported stinging; P = 0.007
Fusidic acid 1% viscous drops twice daily *v* chloramphenicol 0.5% drops 4-hourly [35]	541	Over 1 year	17% culture-positive	Not reported	Success of treatment, assessed by investigator: 96% with fusidic acid *v* 97% with chloramphenicol cured; P = 0.56; complete absence of symptoms: 71% with fusidic acid *v* 77% with chloramphenicol; P = 0.14	11% with fusidic acid *v* 37% with chloramphenicol reported bad taste; P = 0.001
Fusidic acid 1% viscous drops twice daily after loading dose *v* chloramphenicol 0.5% drops 6 times daily after loading dose [36]	340	Adults and children (ratio not specified)	161/340 (47%) culture-positive	Not reported	greater than 90% cured/improved; median: 6.6 days with fusidic acid *v* 6.2 days with chloramphenicol. No significant difference between fusidic acid and chloramphenicol	31% with fusidic acid *v* 16% with chloramphenicol reported itching, burning, blurred vision, bad taste

Intervention	Number of participants	Age of participants	Proportion culture-positive	Microbiological cure rate	Clinical cure rate	Adverse effects
Fusidic acid 1% suspension in carbomer gel twice daily after loading dose *v* chloramphenicol 0.5% drops 5–6 times daily after loading dose [37]	250	221 adults (16–89 years), 29 children (1–14 years)	Not all culture-proved	Not reported	84% with fusidic acid *v* 81% with chloramphenicol cured (mean: 3.3 days with fusidic acid *v* 3.6 days with chloramphenicol); P = NS	5% with fusidic acid *v* 14% with chloramphenicol reported mild to moderate itching, stinging, local discomfort
Fusidic acid viscous drops 1% twice daily for 5–7 days *v* chloramphenicol 1% ointment 3-hourly [39]	505 recruited; 16 lost to follow-up	1–90 years	27% of 486 culture-positive for pathogenic bacteria	Not reported	83% with fusidic acid *v* 84% with chloramphenicol; P = NS	15% fusidic acid *v* 11% chloramphenicol (smarting, irritation, stinging, red eye, blurred vision). Treatment discontinuation because of adverse effects greater with chloramphenicol (P less than 0.01)
Lomefloxacin 0.3% drops twice daily *v* norfloxacin 0.3% 4 times daily [25]	145	Age not specified	27% culture-positive	No significant difference in reduction of bacterial counts between lomefloxacin and norfloxacin. By day 7–9, colony count score reduced by 96% with lomefloxacin *v* 85% with norfloxacin (P = 0.47)	No significant difference in reduction of signs and symptoms at 7–9 days between lomefloxacin and norfloxacin; clinical scores reduced by 96% with lomefloxacin *v* 90% with norfloxacin (P greater than 0.4)	12 with lomefloxacin *v* 14 with norfloxacin (more burning with norfloxacin)
Lomefloxacin 0.3% drops twice daily after loading dose *v* chloramphenicol 0.5% drops 5 times daily after loading dose [26]	191	16–85 years	96/191 culture-positive	No significant difference between lomefloxacin and chloramphenicol by 3–5 days, 0 colonies in 79% with lomefloxacin *v* 80% with chloramphenicol; no significant difference in colony count scores by 3–5 days (P = 0.97) or at days 7–9 (P = 0.12)	No significant difference between lomefloxacin and chloramphenicol in the cumulative score of signs and symptoms in people with bacteriologically confirmed (at 3–5 days P = 0.83; at 7–9 days P = 0.18) or clinically diagnosed (3–5 days P = 0.54; 7–9 days P = 0.63) bacterial conjunctivitis	Good to excellent tolerance rating
Lomefloxacin 0.3% drops twice daily *v* gentamicin 0.3% drops 4 times daily after loading dose [22]	66	8–80 years	46% culture-positive	Most positive cultures were eradicated by days 3–5, with no significant difference between lomefloxacin and gentamicin. By days 3–5, positive cultures eradicated in 21/32 with lomefloxacin *v* 27/32 with gentamicin (P = 0.91)	In people with culture-positive bacterial conjunctivitis, no significant difference in clinical scores at 7–9 days between lomefloxacin and gentamicin (reduced by 82% with lomefloxacin *v* 78% with gentamicin; P = 0.58). In people with clinically diagnosed bacterial conjunctivitis, clinical scores reduced by 78% with lomefloxacin *v* 73% with gentamicin (P = 0.58) at 7–9 days	Adverse events: 1 with lomefloxacin *v* 3 with gentamicin (more burning with gentamicin)
Lomefloxacin 0.3% twice daily *v* tobramycin 0.3% 4 times daily [29]	99 recruited, 92 completed	Mean age 42 years; range 11–80 years	About 50%	At days 1 and 2: 48% with lomefloxacin *v* 55% with tobramycin; At days 7 and 8: 23% with lomefloxacin *v* 36% with tobramycin (reported as NS; P value not reported)	Not reported	Similar rates and duration of burning sensation after instillation in both groups
Lomefloxacin 0.3% drops *v* fusidic acid 1% gel twice daily after loading dose [34]	45	Adults and children (ratio not specified)	81% culture-positive	Eradicated at days 3–5: 8/15 (53%) with lomefloxacin *v* 4/16 (25%) with fusidic acid; P = 0.075	No significant difference between lomefloxacin and fusidic acid in reduction of signs and symptoms (reported as NS, absolute results presented graphically)	Significantly more people using fusidic acid had burning (11% with lomefloxacin *v* 48% with fusidic acid; P = 0.009)

Intervention	Number of participants	Age of participants	Proportion culture-positive	Microbiological cure rate	Clinical cure rate	Adverse effects
Tobramycin 0.3% drops, 1–2 drops 4 to 6 times daily *v* fusidic acid 1% viscous drops, 1 drop twice daily for 7 days [38]	494 recruited; 487 treated; 8 people lost to follow-up; information provided only for subgroup with pathogenic bacteria	2–85 years. Cohort was subdivided into 2 groups (2–9 years and over 9 years)	66% culture-positive, but 70% of culture-positive people had normal flora on quantitative microbiology	No significant difference between fusidic acid and tobramycin after 7 days' treatment (81% with fusidic acid *v* 88% with tobramycin; P = 0.34)	No significant difference in signs and symptoms at 7 days. In children aged 2–9 years: 77% with fusidic acid *v* 83% with tobramycin; In people aged over 9 years: 76% with fusidic acid *v* 73% with tobramycin (reported as NS; P value not reported)	Fusidic acid 4% (tearing, burning, irritation, stinging, allergic reaction, conjunctival injection), tobramycin 2% (irritation, pain, red eye, photosensitivity, discharge; P value not reported); 2 people withdrawn from each treatment group because of adverse effects
Combination of trimethoprim (5 mg/g) and polymyxin B sulphate (10,000 U/g) *v* chloramphenicol (10 mg/g) as ointment 4 times daily [30]	42	Adults and children (ratio not specified)	55% culture-positive	Eradicated: 13/16 (81%) with trimethoprim–polymyxin B sulphate *v* 4/9 (44%) with chloramphenicol; P value not reported	88% with trimethoprim–polymyxin B sulphate *v* 71% with chloramphenicol had greater than 90% reduction in signs and symptoms at day 10; 100% with trimethoprim–polymyxin B sulphate *v* 94% with chloramphenicol with greater than 50% reduction (P = NS)	3 people using trimethoprim–polymyxin B sulphate reported stinging, grittiness, conjunctival hyperaemia, or lid oedema
Combination of trimethoprim (1 mg/mL) and polymyxin B sulphate (10,000 U/mL) *v* chloramphenicol drops 6 times daily for 7 days [31]	40	8–70 years (ratio not specified)	95% culture-positive	Not reported	No significant difference between trimethoprim–polymyxin B sulphate and chloramphenicol in reduction in signs/symptoms score at 7 days (56% with trimethoprim–polymyxin B sulphate *v* 57% with chloramphenicol; reported as NS; P value not reported)	Adverse effects not assessed in the RCT
Combination of trimethoprim (1 mg/mL) plus polymyxin B sulphate (10,000 U/mL) drops *v* chloramphenicol (5 mg/mL) 4 times daily. [32] Multicentre trial with 2 separate comparisons (other comparison reported below)	130	Adults and children (ratio not specified)	43% culture-positive	Eradicated: 19/24 (79%) with trimethoprim–polymyxin B sulphate *v* 21/26 (81%) with chloramphenicol	74% with trimethoprim–polymyxin B sulphate *v* 54% with chloramphenicol had greater than 90% reduction in signs and symptoms at days 10–14 (P = NS); 95% with trimethoprim–polymyxin B sulphate *v* 85% with chloramphenicol had greater than 50% reduction (P = NS)	4 withdrawals from study because of stinging *v* 3 withdrawals because of allergic reaction
Combination of trimethoprim (1 mg/mL) plus polymyxin B sulphate (10,000 U/mL) drops *v* combination of polymyxin B sulphate (5000 U/mL) plus neomycin (1700 U/mL) plus gramicidin (25 U/mL) 4 times daily. [32] Multicentre trial with 2 separate comparisons (other comparison reported above)	100	Adults and children (ratio not specified)	43% culture-positive	Eradicated: 15/27 (56%) with trimethoprim–polymyxin B sulphate *v* 18/33 (55%) with polymyxin B sulphate	80% with trimethoprim–polymyxin B sulphate *v* 68% with polymyxin B sulphate–neomycin–gramicidin; greater than 90% reduction in signs and symptoms at days 10–14 (P greater than 0.05); 96% with with trimethoprim–polymyxin B sulphate *v* 88% with polymyxin B sulphate–neomycin–gramicidin had greater than 50% reduction in signs and symptoms (P = NS)	See trimethoprim–polymyxin B sulphate group adverse events above; 1 withdrawal from polymyxin B sulphate group because of periorbital oedema
Trimethoprim–polymyxin B sulphate drops *v* neomycin–polymyxin B sulphate–gramicidin drops 6 times daily [33]	48	Adults and children (ratio not specified)	46% culture-positive	Eradicated in 8/8 (100%) with trimethoprim–polymyxin B sulphate *v* 12/14 (86%) with neomycin–polymyxin B sulphate–gramicidin	No significant difference in symptoms and signs after 10 days' treatment between trimethoprim–polymyxin B sulphate and neomycin–polymyxin B sulphate–gramicidin (reported as NS; P value not reported; absolute results tabulated)	Adverse effects not assessed in the RCT

Intervention	Number of participants	Age of participants	Proportion culture-positive	Microbiological cure rate	Clinical cure rate	Adverse effects
Combination of trimethoprim (5 mg/g) and polymyxin B sulphate (10,000 U/g) *v* chloramphenicol (10 mg/g) as ointment 3 or 4 times daily (4 separate RCTs of this comparison reported in this article) [21]	448	Adults and children (ratio not specified)	32–72% culture-positive	Not reported	Trial 1: 73% with trimethoprim/polymyxin B sulphate *v* 67% with chloramphenicol cure (P greater than 0.1); trial 2: 65% with trimethoprim/polymyxin B sulphate *v* 42% with chloramphenicol cure (P = 0.1); trial 3: 80% with trimethoprim/polymyxin B sulphate *v* 64% with chloramphenicol cure (P greater than 0.1); trial 4: 37% with trimethoprim/polymyxin B sulphate *v* 50% with chloramphenicol cure (P greater than 0.1) (at 10 days)	22 with trimethoprim–polymyxin B sulphate *v* 12 with chloramphenicol people (stinging, swollen lids, irritation, tearing)
Moxifloxacin 0.5% 1 drop 3 times daily *v* trimethoprim 1%/polymyxin B 10,000 IU 1 drop 4 times daily [40] *Note – trimethoprim/polymyxin B dose is the lowest recommended dose for condition for adults and is lower than that used in most of the other studies of trimethoprim/polymyxin reviewed here. Manufacturer has no recommended paediatric dose	56	1 month–18 years	68/84 eyes (81% of eyes)	Microbiological cure rate at 48 hours was broken down by pathogen isolated and showed significant differences favouring moxifloxacin for all bacterial pathogens	Culture-positive eyes at 48 hours: clinical cure rate 81% with moxifloxacin *v* 44% with trimethoprim/polymyxin; P = 0.001. All eyes at 48 hours: clinical cure rate 88% with moxifloxacin *v* 44% with trimethoprim/polymyxin; P = 0.001 *Note – unit of analysis was not the unit of randomisation	No treatment-related adverse events; 1 episode otitis media in moxifloxacin group and 1 episode respiratory syncytial virus infection in trimethoprim/polymyxin group
Confirmed bacterial conjunctivitis						
Ciprofloxacin 0.3% drops 4-hourly while awake after loading dose *v* tobramycin 0.3% drops 4-hourly while awake after loading dose [47]	241	Age unspecified	Culture-proved	Eradication or reduction: 94% with ciprofloxacin *v* 92% with tobramycin (P = 0.5)	Not reported	Adverse effects not assessed in the RCT
Ciprofloxacin 0.3% drops 2-hourly for 2 days then 4 times daily for 5 more days *v* tobramycin drops 2-hourly for 2 days then 4 times daily for 5 more days [55]	257 (only 141 evaluated for efficacy, but all evaluated for safety)	0–12 years	100% culture-positive	Eradicated: 90% with ciprofloxacin *v* 84% with tobramycin; P = 0.29	Cured by investigator assessment on day 7: 87% with ciprofloxacin *v* 89.9% with tobramycin (P = 0.6)	3 people in each group had adverse effects (dry eye, pruritus, lid oedema, leukoderma, hyperaemia; significance not calculated); 2 people using tobramycin withdrew as a result
Fusidic acid 1% gel *v* chloramphenicol 0.5% drops 4 to 6 times daily for 7 days [54]	139 (114 with fusidic acid *v* 25 with chloramphenicol) (248 total, but only the 139 culture-positive patients used to calculated success rates)	up to 15 years	100% culture-positive (56% of the total 248)	Not reported (resistance: 16% with fusidic acid *v* 55% with chloramphenicol; statistical analysis not provided)	85% with fusidic acid *v* 48% with chloramphenicol; P less than 0.0001	No adverse events associated with treatment reported by participants

Intervention	Number of participants	Age of participants	Proportion culture-positive	Microbiological cure rate	Clinical cure rate	Adverse effects
Levofloxacin 0.5% *v* ofloxacin 0.3% [59]	423 recruited; 208 people included in efficacy analysis	1–91 years	100%	At final visit (6–10 days after start of treatment): 89% with levofloxacin *v* 80% with ofloxacin; P = 0.034 At end point (defined as last observation, up to and including day 10 after start of treatment): 90% with levofloxacin *v* 81% with ofloxacin; P = 0.038	Cured at end point (defined as last observation, up to and including day 10 after start of treatment): 76% in each group; P greater than 0.05	Burning: 1.45% with levofloxacin *v* 0.97% with ofloxacin; other adverse effects not examined
Levofloxacin 0.3% *v* ofloxacin 0.3% [60]	132 (72 with culture-confirmed bacterial conjunctivitis)	18–65 years	100%	Not reported	Similar cure rates at end of study: 97% with levofloxacin *v* 94% with ofloxacin either completely or obviously improved; P value not reported. No significant difference in number of days until improved (mean: 4.89 days with levofloxacin *v* 5.13 with ofloxacin; P greater than 0.05)	2 people using levofloxacin and 1 using ofloxacin had slight irritation
Lomefloxacin 0.3%, 1 drop 2-hourly on day 1 then twice daily for 1 week *v* ofloxacin 0.3% 4 times daily for 1 week [57]	45 entered, 40 completed	Mean 30 years; range 1–78 years	100%	Not reported	88% with lomefloxacin *v* 75% with ofloxacin; P less than 0.08	1 person in each group reported burning sensation after instillation
Netilmicin *v* gentamicin, 1–2 drops 4 times daily for up to 10 days [58]	209 recruited; 121 analysed, all of whom were culture-positive at baseline	Mean (± SD) 49 ± 19 years	100% of those analysed were culture-positive	Netilmicin significantly more effective than gentamicin at 5 days (P = 0.001) and 10 days (P = 0.037); absolute results presented graphically	Netilmicin significantly more effective than gentamicin at 3 days (P = 0.037), 5 days (P = 0.001), and 10 days (P = 0.001); absolute results presented graphically	2% with netilmicin *v* 4% with gentamicin (adverse events included redness, itching, and burning)
Trimethoprim hemisulphate 1.0 mg/mL plus polymyxin B sulphate 10,000 U/mL *v* gentamicin sulphate 3 mg/mL *v* sulfacetamide 100 mg/mL;all for 10 days [56]	158	2 months–22 years	100% culture-positive for *H influenzae* or *S pneumoniae*	At 2–7 days after treatment: 83% with trimethoprim–polymyxin B sulphate *v* 68% with gentamicin *v* 72% with sulfacetamide; P = NS	At 2–7 days after treatment: 84% with trimethoprim–polymyxin B sulphate *v* 88% with gentamicin *v* 89% with sulfacetamide; P = NS	Similar safety profiles
Levofloxacin 0.5% 1 drop 3 times daily *v* levofloxacin 0.5% 1 drop 2-hourly on days 1 and 2 then 1 drop 4-hourly on days 3–5 (usual dosing). [63]	86 (119 originally enrolled, but 27 had negative bacteriological results)	18–70 years	72%	93% with 3-times-daily dosing *v* 96% in usual dosing; P = 1.00, NS	85% with 3-times-daily dosing *v* 92% in usual dosing; P = 0.48, NS	The RCT reported no adverse events in the studied groups
Azithromycin 1.5% 1 drop twice daily for 3 days *v* tobramycin 0.3% 1 drop 2-hourly for 2 days then 4 times daily for 5 days. [61] [62]	1043 subjects randomised (ITT set), 1015 in safety set (all "evaluable" subjects who got medication), 521 in modified ITT set (culture-positive), and 417 in per-protocol set (no protocol deviations)	4 days–87 years	50% (51.5% for azithromycin and 48.4% for tobramycin)	Bacterial resolution on worse eye only (or right eye if equal severity) in per-protocol set: At day 3: 85% with azithromycin *v* 84% with tobramycin (difference +1.4%, 95% CI –5.3% to +8.3%) At day 9: 93% with azithromycin *v* 95% with tobramycin (difference –1.8%, 95% CI –6.6% to +3.0%)	Clinical cure at 9 days: Per-protocol set: 88% with azithromycin *v* 89% with tobramycin (ARD +1.6%, 95% CI –7.5% to +4.4%) Modified ITT set: 86% with azithromycin *v* 86% with tobramycin (ARD +0.5%, 95% CI –6.6% to +5.8%) ITT set: 85% azithromycin *v* 85% tobramycin (ARD: +0.5%, 95% CI –3.8% to +4.9%)	Adverse events mild to moderate only: 3/508 (0.5%) reported effects related with azithromycin (burning, foreign body sensation) and 2 discontinued the study; 1/502 (0.1%) reported discharge with tobramycin
Topical versus oral antibiotics						

Intervention	Number of participants	Age of participants	Proportion culture-positive	Microbiological cure rate	Clinical cure rate	Adverse effects
Suspected bacterial conjunctivitis						
Polymyxin B sulphate bacitracin 4 times daily for 7 days *v* oral cefixime 8 mg/kg daily for 3 days [41]	80	2 months–6 years	70% culture-positive	Bacteriological failure at 3 days: 18% with polymyxin B sulphate bacitracin *v* 38% with cefixime; P = 0.07	Not stated but difference reported as NS	Adverse effects not assessed in the RCT

Antibiotic dosing ranges in this table may vary from the usual clinical recommendations for mild conjunctivitis. However, they are within the accepted ranges for clinician-directed treatment of conjunctivitis based on severity as recommended in major pharmacotherapeutic reference databases.
ARI, absolute risk increase; SD, standardised difference; NS, not significant; ITT, intention to treat; ARD, absolute risk difference.

TABLE **GRADE evaluation of interventions for bacterial conjunctivitis**

Important outcomes					Cure rates, adverse effects				
Number of studies (participants)	Outcome	Comparison	Type of evidence	Quality	Consistency	Directness	Effect size	GRADE	Comment
What are the effects of empirical treatment in adults and children with suspected bacterial conjunctivitis?									
4 (1098) [18] [19] [20] [11]	Cure rates	Topical antibiotics *v* placebo or no immediate treatment	4	−1	−1	0	0	Low	Quality point deducted for self-report of clinical cure by parents in 1 RCT. Consistency point deducted for conflicting results
20 (at least 597) [22] [23] [24] [21] [25] [26] [27] [28] [29] [30] [31] [32] [33] [34] [35] [36] [37] [38] [39] [40]	Cure rates	Topical antibiotics *v* each other	4	−2	0	0	0	Low	Quality points deducted for incomplete reporting of results and for weak methods in some RCTs
1 (80) [41]	Cure rates	Topical *v* oral antibiotics	4	−2	0	−1	0	Very low	Quality points deducted for sparse data and incomplete reporting of results. Directness point deducted for small number of comparators
1 (104) [42]	Cure rates	Different regimens of topical antibiotics *v* each other	4	−1	0	−1	0	Low	Quality point deducted for sparse data. Directness point deducted for small number of comparators
What are the effects of treatment in adults and children with bacteriologically confirmed bacterial conjunctivitis?									
8 (1933) [46] [47] [48] [49] [51] [52] [53]	Cure rates	Topical antibiotics *v* placebo	4	0	0	−1	0	Moderate	Directness point deducted for uncertainty about generalisability of results (to situations where treatment not initiated until culture results are known, because of the delay in treatment)
9 (at least 1584) [47] [54] [55] [56] [57] [58] [59] [60] [61]	Cure rates	Topical antibiotics *v* each other	4	−1	−1	0	0	Low	Quality point deducted for incomplete reporting of results. Consistency point deducted for inconsistent results between RCTs
1 (86) [63]	Cure rates	Different regimens of topical antibiotics *v* each other	4	−1	0	−1	0	Low	Quality point deducted for sparse data. Directness point deducted for small number of comparators
What are the effects of treatment in adults and children with clinically confirmed gonococcal conjunctivitis?									
4 (239) [64] [65]	Cure rates	Parenteral antibiotics plus topical antibiotics *v* parenteral antibiotics alone or *v* parenteral antibiotics plus different topical antibiotic	4	−1	−1	−1	0	Very low	Quality point deducted for incomplete reporting of results. Consistency point deducted for conflicting results. Directness point deducted for all studies in Africa, which may affect generalisability

Type of evidence: 4 = RCT. Consistency: similarity of results across studies
Directness: generalisability of population or outcomes
Effect size: based on relative risk or odds ratio